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The Journal of General Physiology

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Volume 130, 2007

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The Journal of General Physiology
Vol 130 • No 1 • July 2007

General Physiology is the study of biological mechanisms through analytical investigations, which decipher the molecular and cellular mechanisms underlying biological function at all levels of organization.

The mission of the *Journal of General Physiology* is to publish articles that elucidate important biological, chemical, or physical mechanisms of broad physiological significance.

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Cover picture: Generation of cone pigment knock-in mice. (Left) Retinal sections of wild type (Rh/Rh), heterozygote (Rh/mG) and homozygote (mG/mG), showing replacement of rhodopsin with mouse green-sensitive cone pigment (mGreen). (Middle) Response curves for Rh/Rh (top) and mG/mG (below) rods. (Right) Mouse green-containing rods have lower sensitivity (top) and amplification constant (below) (see article by Sakurai et al., 21–40).

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The Journal of General Physiology
Vol 130 • No 2 • August 2007

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The Journal of General Physiology
Vol 130 • No 3 • September 2007

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Cover picture: Some ion channels, including KCNQ channels shown here, are sensitive to cytoplasmic Mg^{2+} ions. The current decreases reversibly when cytoplasmic Mg^{2+} is raised and increases when it is lowered (left). The changes can be explained by a model in which Mg^{2+} and polycationic amines bind to plasma membrane PIP_2, decreasing the pool of free PIP_2 needed to keep KCNQ channels active (see article by Suh and Hille, 241–256).

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Vol 130 • No 4 • October 2007

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Cover picture: Only a handful of residues are highly conserved throughout the CLC family. One of these, a lysine residue on helix E (purple), participates in a hydrogen-bond network with residues that directly coordinate the chloride ions in the pore. Mutation of this lysine in ClC-0 causes a shift in the fast-gate voltage dependence but preserves the sensitivity to extracellular chloride (compare bottom two panels). Analysis of gating kinetics in combination with the available structural information suggest some of the structural changes likely to underpin fast-gate opening (see articles by Engh et al., 335–349 and 351–363).

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The Journal of General Physiology
Vol 130 • No 5 • November 2007

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Cover picture: (top) In a mixture of ATP and AMP-PNP, a single molecule of the motor enzyme kinesin-1 makes alternating runs and pauses as it moves along a microtubule. Examples of long and short runs are highlighted. Smaller panels show controls with ATP alone or AMP-PNP alone. (bottom) Proposed movement mechanism showing the two separate catalytic cycles that give rise to the long and short runs. E, microtubule-bound dimeric kinesin; T, ATP; D, ADP; I, AMP-PNP; Pi, inorganic phosphate (see article by Subramanian and Gelles, 445–455).

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The Journal of General Physiology
Vol 130 • No 6 • December 2007

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Cover picture: TPLSM image (top left) and fluorescence intensity profile (top center) of a muscle fiber expressing EGFP-F. Bottom left and center panels display dynamic EGFP-F fluorescence quenching and DiBAC4(5) excited emission signals, respectively. The voltage dependence of these signals and a model of the FRET interaction between DiBAC4(5) and EGFP-F are shown in the bottom and top right panels, respectively (see article by DiFranco et al., 581–600).